Environmental Health Perspectives
Vol. 25, pp. 103-109, 1978

Levels of Lead and Other Metals in Human Blood: Suggestive Relationships, Determining Factors

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Epidemiological studies on metal levels in blood were carried out. Evidence suggested the existence of a different trend in serum-iron levels in relation to blood lead levels in nonoccupationally exposed males (negative trend) and females (positive trend). There was a positive relation between blood lead levels and blood manganese levels in children and occupationally exposed male workers. Blood metal levels increased with age in young children. There was evidence for an influence of socioeconomic class on blood lead levels in children. A direct and an indirect effect of smoking was found on blood lead levels and on the activity of δ-aminolevulinic acid dehydratase activity in erythrocytes in adult nonoccupationally exposed females.

Introduction

This paper presents data from six epidemiological studies on metal levels in blood of human beings. Lead in blood (PbB) levels are regarded as an independent variable. The other metals studied were cadmium (Cd), manganese (Mn), zinc (Zn), copper (Cu), and iron (Fe).

A few studies have already been published fully, other studies are being prepared for publication.

The studies were not designed explicitly to evaluate relationships between Pb and other metal levels, but were carried out for other purposes as explained further on.

The epidemiological studies were carried out on the following groups: study I: nonoccupationally exposed adult males and females; study II: young hospitalized children; study III: 2- and 3-year-old children living around a secondary lead smelter, study IV: workers from a car factory; study V: workers from a cable factory; study VI: workers from a secondary lead smelter.

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Analytical and Statistical Methods

The metals were measured in whole blood by flameless atomic absorption spectrometry procedures worked out by the Coronel Laboratory (*1*). The metal levels in whole blood are indicated as metal-B (e.g., lead in blood = PbB); iron was measured in serum (Fe-S) with colorimetry in an Autoanalyzer (Clinical Laboratory, University Hospital (*2*).

The 95% confidence limits as measured for analytical precision were: ± 40 ppb for PbB < 300 ppb; ± 50 ppb for PbB > 400 ppb; ± 0.7 ppb for CdB < 1.0 ppb; ± 2 ppb for CdB > 2.0 ppb; ± 2 ppb for MnB; ± 0.2 ppm for CuB; ± 2.0 ppm for ZnB < 5 ppm; ± 4.0 ppm for ZnB > 6.0 ppm; ± 2 μmole/l. for Fe-S.

Quality control for measurement of blood metal levels was as follows. On each day of measurement, four deep-frozen blood standards, spiked and unspiked, were analyzed. The laboratory was taking part in interlaboratory comparison studies for PbB analysis at the same time, which offered a further control possibility. Two technicians carried out analysis of the same samples in order to evaluate the technician effect, if any. For PbB, mean levels were

260 and 277 ppb, respectively. For CdB, technician I and technician II measured 11.5 and 11.7 ppb, respectively, whereas the outside laboratory gave a value of 11.0 ppb. No interlaboratory comparison was performed for MnB. For comparison of CdB levels in various studies, see (*3*).

The following statistical methods were used: multiple variance analysis, (log) linear correlation analysis, contrast methods.

Blood Lead and Serum Iron Levels

Study I. Nonoccupationally Exposed Adult Males and Females

This study was designed to explore factors possibly associated with female hypersusceptibility to lead in regard to heme synthesis (*4, 5*). In 1976, PbB, free erythrocyte porphyrin (FEP), Fe-S, total iron binding capacity (TIBC), hemoglobin (Hb) and hematocrit (Hct) were measured in 19–21-year-old male and female medical students.

In May 1976 three groups were examined: 57 males, 47 females not using oral contraceptives and 44 females using oral contraceptives. In November-December 1976, another group of 51 male students of similar age was examined for PbB, Hb, Hct, and Fe-S. The groups are denoted respectively as MI, FNC, FC, MII. In the first group blood was taken in the morning (9:00–10:30 a.m.) from the subjects in a random sequence; samples were analyzed blind. In the last group blood was taken in the afternoon (15:00–16:00 p.m.) for a second measurement of Fe-S. Mean corpuscular hemoglobin concentration (MCHC) and unsaturated iron binding capacity (UIBC) were calculated. The relevant findings are given in Table 1.

The Fe-S values for the MII group averaged 22.0 μmole/l. in the morning and 20.6 μmole/l. in the afternoon. This difference is not significant.

Some of the differences in blood levels were significant between the May 1976 groups (MI, FNC and FC); FEP: MI-FNC ($p < 0.05$); Hb: MI-FNC ($p < 0.001$); MI-FC ($p < 0.001$); Hct: MI-FNC ($p < 0.001$); MI-FC ($p < 0.001$); MCHC: MI-FNC ($p < 0.05$); MI-FC ($p < 0.05$); Fe-S: MI-FNC ($p < 0.01$); FNC-FC ($p < 0.001$); TIBC: FNC-FC ($p < 0.001$); UIBC: MI-FNC ($p < 0.01$), FNC-FC ($p < 0.05$).

Within the groups, the following correlations were observed: MI: PbB-Fe-S ($p < 0.01$), $r = -0.36$; MII: $r = -0.14$ ($0.05 < p < 0.10$); FNC + FC ($p < 0.05$): $r = +0.25$.

In summary, the results show that Hb, Hct, and MCHC are higher in males than in females, whereas FEP is higher in females than in males at same levels of PbB. In females not using oral contraceptives Fe-S is lower than in males; in females using oral contraceptives Fe-S is higher than in females not doing so. In males there exists a negative correlation between PbB and Fe-S. In females there is a trend toward a positive correlation. There is a significant positive correlation if FNC and FC are combined. TIBC is higher in males than in females not using oral contraceptives. UIBC is lower in males than in females not using oral contraceptives. The use of oral contraceptives leads to higher Fe-S, higher TIBC and lower UIBC.

Neither the type of oral contraceptives nor the day in the menstrual cycle had an influence on the Fe-S levels. The oral contraceptives used were mainly Microgynon (34%), Neogynon (16%), Stederyl (11%), and Orthonovum (11%).

Studies V and VI. Workers from a Cable Factory and from a Secondary Lead Smelter

Both studies were carried out to assess exposure to lead compounds by means of biological monitoring.

In a cable factory where lead compounds were used as stabilizers, resulting in a slight exposure to lead, no relation between PbB and Fe-S was ob-

Table 1. Arithmetic average and standard deviation of blood parameters (for FEP geometric average and range) in nonoccupationally exposed males and females.

Parameter	MI, $n = 57$	MII, $n = 51$	FNC, $n = 45(47)$	FC, $n = 43(44)$
PbB, ppb	138 ± 39	112 ± 31	130 ± 42	143 ± 38
FEP, μg/100 ml rbc	33.1 (25.1–43.7)	—	37.2 (26.3–52.5)	36.3 (26.9–49.0)
Hb, mmole/l.	10.0 ± 0.5	10.1 ± 0.5	8.9 ± 0.6	8.9 ± 0.5
Hct, %	45.4 ± 2.4	47.1 ± 2.5	41.2 ± 2.3	40.9 ± 2.3
MCHC, mmole/l.	22.0 ± 0.6	21.5 ± 0.7	21.7 ± 0.6	21.7 ± 0.6
Fe-S, μmole/l.	22.1 ± 7.8	22.0 ± 7.9	18.4 ± 6.5	24.0 ± 7.3
TIBC, μmole/l.	62.8 ± 6.4	61.5 ± 7.5	63.6 ± 9.8	72.6 ± 63.3
UIBC, %	64.7 ± 12.3	64.1 ± 12.1	71.0 ± 9.7	66.4 ± 10.5

served in 34 men whose PbB values with one exception were less than 300 ppb (study V). No relation was found between these two parameters in 111 male secondary smelter workers whose main task was in the refining of accumulator castings. Their PbB values were less than 900 ppb (study VI). It should be noted that no fixed time of blood collection could be adhered to in these studies.

Discussion

It is well known that Fe-S is elevated in subjects with lead poisoning (*7*). In the study of workers with slight to moderate exposure to lead and with PbB below 900 ppb, no relation between PbB and Fe-S was observed. This is not in contradiction with the studies in workers with lead poisoning. A negative association between PbB and Fe-S levels was observed in nonoccupationally exposed males and a positive association in nonoccupationally exposed females (Pb < 240 ppb).

The studies by Stuik (*4*) and Roels et al. (*5*) led to the finding that females were more susceptible to lead then males in regard to protoporphyrin formation in erythrocytes. One could suggest the hypothesis that decreased "availability" of iron might be a factor in explaining this difference assuming that Fe-S levels would predict to a certain extent this availability. Fe-S levels were lower in females not using oral contraceptives than in males, but higher in females using these than in females not using oral contraceptives. Moreover the association between PbB and Fe-S in females showed an opposite trend to that seen in males. Females not using oral contraceptives had the same FEP levels as females using these. However, Fe-S measures only transport of iron (by transferrin) in blood; serum iron is not necessarily a good indicator of iron availability or body stores.

The above observations do not lend support to the hypothesis that differences in iron metabolism, at least in as much as Fe-S levels are concerned, between males and females will be responsible for the sex-linked difference in susceptibility of porphyrin synthesis during exposure to lead. Difference in the endocrine system may be more important.

Wibowo et al. (*6*) suggested two hypotheses to explain the negative relation between PbB and Fe-S levels in nonoccupationally exposed males: (A) competitive binding of lead and iron to transferrin, the iron-transport medium in serum. However, this can explain a negative association only to a limited extent, because over 90% of lead in blood is bound to erythrocytes. (B) A negative feedback of heme on iron-transport through the erythrocyte precursor membrane. With increasing lead concentration in the cell less heme will be produced. This could increase iron transport through the erythrocyte membrane. The suggested mechanisms could work simultaneously.

Relationships between lead and iron-metabolism have been reported repeatedly. An iron deficient diet in rats leads to increased enteral absorption and increased retention of lead in liver, kidney and bone marrow (*8*). Conflicting reports exist on the value of iron-therapy in pica (*9, 10*). Delves, Bicknell, and Clayton (*11*) observed a negative correlation between PbB and FeB (i.e., in whole blood) in children suspected of having lead poisoning. In a double-blind study in seven pairs of preschool children Angle, Stelmak and McIntire (*12*) observed in six pairs a larger ($p = 0.06$) increase of PbB in children given an iron-supplementation (200 mg $FeSO_4$/day) than in placebo-treated controls. These data suggest facilitation of lead-absorption (or changed distribution) by oral iron, which is in disagreement with the animal studies (*8*).

Blood Lead and Manganese Levels

Study II. Young Hospitalized Children

This study was designed to give a first exploration of blood metal levels in Dutch children.

In 1975 lead, cadmium, zinc, manganese and copper levels in whole blood were measured in 48 patients (2 months–6 years of age) at the University Children's Hospital, Amsterdam (*13*). The levels are presented in Table 2. There existed a significant positive relationship between age and PbB ($r = 0.44, p < 0.05$) and between age and MnB ($r = 0.40$, $p < 0.05$). The coefficient of correlation between PbB and MnB levels was 0.53 ($p < 0.001$). When

Table 2. Blood metal levels in hospitalized young children (± 1 S.D.).

	Metal Concn				
	0–3 yr		4–6 yr		95% Confidence
Metal	*n*	Level	*n*	Level	limits
Pb, ppb[a]	29	119 (74–191)	19	155 (97–249)	± 40 ppb
Cd, ppb[a]	26	2.36 (1.30–4.27)	19	2.16 (0.96–4.79)	± 2 ppb
Mn, ppb	23	16.9 (10.0–23.8)	12	20.1 (10.6–29.6)	± 2 ppb
Cu, ppm	29	1.03 (0.71–1.31)	19	1.14 (0.87–1.41)	± 0.2 ppm
Zn, ppm	29	4.51 (3.13–5.89)	19	5.25 (3.36–7.41)	± 2 ppm

[a] Geometric average.

age was kept constant, the coefficient of correlation between PbB and MnB was 0.45 ($p < 0.01$).

The objective of this study was not to examine interrelationships. The relations observed cannot yet be accepted as adequately valid. There were too many different diagnoses to elucidate the influence of disease on blood metal levels.

In study II MnB levels were about twice as high as in subsequent studies. This does not invalidate the relationships observed within the group studied.

Study III. Two- and Three-Year-Olds

The study was undertaken to examine the relationship between lead and cadmium in blood levels and residence around a secondary smelter. This smelter emitted mainly lead, a much smaller amount of cadmium, and possibly a small amount of manganese. In the ambient air iron and manganese were present in large particles, whereas lead and cadmium were present in small particles. The first two metals were deposited in the immediate vicinity of the source.

At the end of 1976 we examined PbB, CdB, MnB, ZnB, FEP, Hb and Hct values in 108 two- and three-year-old children. The levels observed in relation to distance from source are given in Table 3.

The children were divided into two socioeconomic classes, according to the parents' occupation: SEC I, white collar, SEC II, blue collar. In children living more than 2 km from the source mean PbB levels were 104 ppb for SEC I ($n = 21$) and 134 ppb for SEC II ($n = 14$). In children living less than 2 km from the source mean PbB was 137 ppb in SEC I ($n = 24$) and 165 ppb in SEC II ($n = 39$). Two-way variance analysis showed that the difference in PbB levels, 20–30 ppb higher in SEC II than in SEC I, was independent of distance ($p > 0.1$). The difference between SEC I and SEC II was significant at $p < 0.05$. There was no effect of SEC on the other parameters measured.

The relationship between PbB and the other parameters measured is given in Table 4. Mean MnB levels are higher when PbB levels are above 150 ppb than when PbB levels are below 150 ppb. There was no decrease of MnB levels with increasing distance from source.

Study IV. Workers from a Car Factory

In 1976, lead and manganese levels in blood of 13 workers from a car factory were measured in order to assess total exposure to lead, when spraying paint, polishing car bodies, etc. According to management there was no exposure to manganese. The PbB levels ranged from 148 to 772 ppb, the MnB levels from 5.6 to 15.9 ppb. The coefficient of correlation between PbB and MnB was 0.58 ($p < 0.05$). There was no relation between PbB and Hb or Hct.

This study again suggests that with increasing PbB levels MnB levels may also increase, since simultaneous occupational exposure to lead and managanese probably did not exist.

Table 3. Blood levels of lead, manganese, cadmium, and zinc and blood parameters in two- and three-year-old children in relation to distance from secondary lead smelter (range).

	Metal blood levels (range)		
	Distance < 1 km ($n = 17$)	Distance = 1–2 km ($n = 54$)	Distance > 2 km ($n = 37$)
PbB, ppb	196 (123–327)	147 (58–383)	119 (45–262)
MnB, ppb	7.31 (4.2–10.4)	7.2 (3.6–11.9)	7.5 (2.7–14.1)
CdB, ppb	0.9 (0.2–2.1)	0.8 (0.3–3.5)	0.8 (0.2–1.8)
ZnB, ppm	4.4 (3.1–5.7)	4.9 (2.0–9.7)	4.7 (2.5–9.1)
FEP, μg/100 ml rbc	42.0 (17.2–82.2)	38.1 (17.8–138.9)	33.6 (10.5–84.8)
Hb, mmole/l.	8.0 (6.4–9.1)	8.0 (6.8–9.2)	8.0 (6.2–9.0)
Hct, %	37 (28–43)	37 (31–43)	38 (29–43)

Table 4. Blood levels of manganese, cadmium, and zinc and blood parameters in two- and three-year-old children in relation to PbB levels, mean values (and range).

	PbB < 100 ppb, $n = 17$	PbB = 101–150 ppb, $n = 34$	PbB = 151–200 ppb, $n = 38$	PbB = 201–250 ppb, $n = 7$	PbB > 250 ppb, $n = 9$
MnB, ppb	6.9 (3.6–10.5)	6.8 (2.7–13.3)	7.7 (4.0–14.1)	8.1 (6.0–10.8)	8.0 (5.0–10.0)
CdB, ppb[a]	0.68 (8.3–1.6)	0.62 (0.2–1.5)	0.66 (0.2–1.5)	0.65 (0.4–1.8)	1.17 (0.5–3.5)
ZnB, ppm	5.4 (3.9–7.6)	4.6 (2.9–6.0)	4.8 (2.0–9.1)	4.8 (3.3–5.4)	4.3 (3.2–5.2)
FEP, μg/100 ml rbc)[a]	33.8 (20.1–48.8)	34.7 (17.1–68.2)	37.2 (10.5–84.8)	49.0 (17.2–99.9)	59.0 (34.6–138.0)
Hb, mmole/l.	8.0 (6.9–9.0)	7.9 (6.2–8.9)	8.1 (6.8–9.3)	7.8 (6.4–8.9)	8.1 (7.5–8.7)
Hct, %	37 (31–40)	37 (29–42)	38 (33–43)	36 (28–42)	38 (35–42)

[a] Geometric mean.

Study V. Workers from a Cable Factory

In April 1977 male workers from a cable factory were examined to assess total exposure to lead. They were exposed to lead containing stabilizers, but not to manganese. PbB levels ranged from 67 to 300 ppb, except in one subject who had 447 ppb. There was no relation between PbB and Fe-S levels in 34 subjects examined, nor between PbB and MnB levels in 24 subjects examined (Table 5).

Table 5. Lead, iron, and manganese levels in blood or serum in workers from a cable factory.

	PbB < 200 ppb			PbB > 200 ppb		
	Level	Range	*n*	Level	Range	*n*
FeS, μmole/l.	24.4	(10.0–37.5)	23	22.6	(14.5–32.0)	11
MnB, ppb	7.2	(4.4–9.3)	17	7.2	(5.5–9.6)	7

Study VI. Workers from a Secondary Lead Smelter

In May 1977 111 workers from a secondary lead smelter (same as in study III) were examined to assess total exposure to lead. The data on PbB, Fe-S, and MnB levels are presented in Table 6.

There was no relationship between PbB and Fe-S levels, but again with increasing PbB there was an increase of MnB: $r = 0.32$, $p < 0.01$. In this group increased occupational exposure to manganese along with lead exposure was unlikely, but could not be excluded.

Table 6. Lead, iron, and manganese levels in blood or serum in 111 workers from a secondary smelter (range).

PbB, ppb	*n*	Fe-S, μmole/l.	MnB, ppb
101–200	5	27.4 (13.0–41.0)	7.7 (2.6–10.8)
201–300	12	26.4 (18.0–42.0)	7.1 (3.8–9.2)
301–400	19	24.8 (17.0–42.0)	9.6 (5.9–14.5)
401–500	18	25.7 (16.0–46.0)	11.4 (4.3–20.3)
501–600	33	25.6 (14.5–44.0)	11.2 (2.9–19.6)
601–700	14	24.5 (16.5–41.0)	10.4 (6.5–15.5)
701–800	9	27.9 (17.5–35.0)	12.5 (7.5–15.0)
801–900	1	22.0	7.4

Discussion

Studies II, III, IV, V, and VI were not designed to elucidate the relation between PbB and MnB levels. It was not possible to carry out a complete environmental monitoring programme for lead and manganese. Therefore, simultaneous exposure to lead and manganese could not be excluded, although such was not likely the case. With the exception of study V (with a small range of PbB levels and a small number of workers) the studies, carried out on subjects widely different in age and in exposure to lead, suggest an increase of MnB levels with increasing PbB levels.

Delves, Bicknell, and Clayton (*11*) studied MnB levels in blood of 91 hospital in-patients between 4 and 15 years of age and of 189 children (2 months to 15 years of age) suspected of having lead poisoning. In the first group, to a certain extent similar to those of study II, they did not find any correlation between PbB and MnB, but in the second group a positive correlation was observed (PbB = 10–1400 ppb, MnB = 18–150 ppb). The increased level of manganese, zinc, strontium, cadmium, and chromium was thought to be due to some simultaneous exposure, maybe pica. In view of the results of our studies a biologic mechanism can also be suggested.

Studies II, III, IV, and VI do not allow a definite conclusion. They may serve to motivate further experimental and epidemiological studies, if possible with concomitant measurement of environmental exposure.

Blood Lead in Relation to Other Metal Levels, Age, and Smoking

In the studies presented, suggestive evidence is given for relations between levels of lead and levels of other metals in whole blood. In two studies the relation between lead in blood and age or environmental conditions was also evaluated. In study II on young hospitalized children there was a positive correlation between age and PbB ($r = 0.44$, $p < 0.05$), age and MnB ($r = 0.40$, $p < 0.05$), age and ZnB ($r = 0.30$, $p < 0.05$), PbB and ZnB ($r = 0.31$, $p < 0.05$), and CdB and ZnB ($r = 0.42$, $p < 0.01$). When age was kept constant, the coefficient of correlation for PbB and ZnB was 0.37 ($p < 0.05$) and for PbB and MnB 0.45 ($p < 0.01$).

In study III on two- and three-year-old children living at various distances from a smelter, there was a correlation between PbB and CdB ($r = 0.34$, $p < 0.0005$). Both PbB and CdB reached their highest levels in those living at a distance of < 1 km. In children with PbB above 150 ppb mean MnB levels were higher than in children with lower PbB levels.

In study I on male and female students we also observed an increase of PbB levels with number of cigarettes smoked per day (*13*) (Table 7).

Table 7. PbB levels as a function of cigarette smoking.

	PbB level, ppb			
	n	Males	*n*	Females
Nonsmokers	36	127 ± 43	54	128 ± 38
1-9 cig/day	8	138 ± 34	23	138 ± 41
10-19 cig/day	7	163 ± 44	11	158 ± 35
≥ 20 cig/day		—	3	190 ± 22

A similar effect of smoking on PbB levels was observed in another study on 222 urban adult females (*3*). In addition we found a large influence of smoking on CdB levels: in nonsmoking females ($n = 84$) $\bar{X}_g = 0.41$ ppb; in those smoking 1-9 cigarettes per day ($n = 61$) $\bar{X}_g = 0.62$ ppb; in those smoking ≥ 10 cigarettes per day ($n = 77$) $\bar{X}_g = 0.70$ ppb.

Recently, we have analyzed the effect of smoking on the level of lead in blood, on δ-aminolevulinic acid dehydratase in erythrocytes and on hematocrit in the same group of 222 females (*15*). The maximum PbB level was 240 ppb. Smoking 10 or more cigarettes per day increases the PbB level directly through increased exposure to Pb and indirectly through increase of Hct. There is an effect of smoking on the lead transport capacity of peripheral blood. Smoking inhibits ALA-D, partly due to an increase of the hematocrit level and partly due to a direct effect on ALA-D, independent of the increase in PbB. It could be calculated that a 65% increase of PbB has the same effect on ALA-D as smoking 10 or more cigarettes per day.

General Discussion

Relationships

This paper presents data for further consideration. We choose PbB levels as the independent variable, and examined the relationship of PbB with other blood metal levels. An association may be due to chance only; to analytical technique; to simultaneous exposure; to the effect of the presence of lead in the gastrointestinal tract on the absorption of other metals, and vice versa; to the presence of a carrier in blood which selectively transports two or more metals; or to the effect of lead on metabolism of other metals, and vice versa.

The epidemiological studies presented were not designed to study the interrelationships as such. Data on exposure through air, food, water, etc. were scanty or nonexistent. Therefore, simultaneous exposure could not be ruled out. The groups examined differed considerably between various studies: males and females; adults and children; occupationally exposed and nonexposed. Nevertheless, suggestive evidence for a relation between blood metal levels, not easily explained by an effect of analytical techniques or of simultaneous exposure, is presented and may well motivate further experimental and epidemiological studies.

Lead and Iron

In studies I, V, and VI we presented data on levels of lead in blood and on serum iron. There appeared to be a different trend between both parameters in nonoccupationally exposed adult males and females: negative in males, positive in females. Very probably there exists an effect of hormones on Fe-S levels. The fact that we did not observe this negative trend between PbB and Fe-S levels in slightly to moderately exposed adult male lead workers (V and VI) does not contradict the finding in the nonoccupationally exposed subjects.

Lead and Manganese

In studies II and III on young children, and in IV, V, and VI on adult male workers, we calculated the relation between lead and manganese levels in blood. The first indication of a positive relation between PbB and MnB levels was presented by Delves, Bicknell, and Clayton (*10*) in their study on children. Except in study V, we found evidence for an increase of MnB levels with increasing PbB levels in our studies, under widely different conditions of age and exposure. The possibility of a chance observation appears to be small. There is no indication of an effect of analytical methods. Simultaneous exposure cannot be ruled out, but in that case one would have expected an effect of distance from the source of pollution in study III (as was the case for CdB), and a larger increase of MnB in study IV and VI in comparison to what was found in studies II and III.

Age

In study II we observed an effect of age on lead, manganese and zinc in blood. This probably reflects—at least partly—increased exposure. An increase of blood metal levels with age in young children has been observed by others (*16–18*).

Socioeconomic Status

In study III we observed an effect of socioeconomic class on levels of lead in blood in young children, but not on the levels of other metals in blood. A similar finding was reported by Landrigan et al. (*17*). This aspect is often neglected in

epidemiological studies. It may reflect increased exposure, but also different metabolism of metals due to, e.g., malnutrition.

Smoking

The effect of smoking on the levels of cadmium in blood is well known. A few authors have also reported increased blood lead levels in smokers (*3*). Usually one does not take into account a direct effect of smoking on the hematocrit. An increased hematocrit level means an increased transport capacity of peripheral blood for erythrocyte-bound metals and may thus cause a positive relation between various blood metal levels. There is reason to correct blood metal levels for hematocrit, if metals are largely bound to red blood cells. Moreover, because of a direct effect of smoking an ALA-D, a study to find out whether a no-effect level of PbB exists for ALA-D inhibition has to be carried out in nonsmokers.

Recommended Studies

The findings of a relation between PbB and Fe-S in nonoccupationally exposed adult subjects, in males and in females with a different trend, need to be confirmed in future studies. The increased susceptibility of the heme synthetic pathways to lead exposure in females appears to be established. The mechanisms underlying this difference deserve further study, particularly in regard to the role of sex hormones.

The suggested relationship between PbB and MnB should be confirmed in experimental and epidemiological studies.

The relationship between blood metal levels and age in young children needs further to be evaluated in relation to the main source of metal uptake.

Studies on interaction of metals should be designed specifically. Data on environmental exposure to the metals under study are necessary.

The effect of socioeconomic class on the PbB level deserves to be studied in regard to possible class dependent variables such as crowding, hygiene, indoor metal levels, and nutrition, to name but a few.

This study was supported by grants from the Dutch Prevention Fund and the Environmental Research Program of the European Economic Community.

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